

WHAT IS CLAIMED IS:

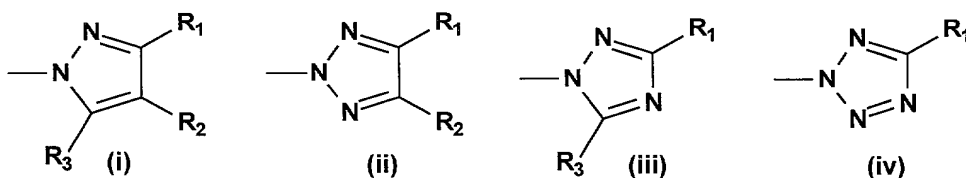
1. A compound having the Formula *I*:



or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is one of O, S, NR<sub>9</sub>, CH<sub>2</sub>, NR<sub>9</sub>C(O), or C(O)NR<sub>9</sub>, where R<sub>9</sub> is hydrogen or C<sub>1</sub>-C<sub>10</sub> alkyl;

Het is a heteroaryl selected from the group consisting of



R<sub>1</sub> is selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted heteroaryl, C(O)R<sub>10</sub>, CH<sub>2</sub>C(O)R<sub>10</sub>, S(O)R<sub>10</sub>, and SO<sub>2</sub>R<sub>10</sub>;

R<sub>2</sub> and R<sub>3</sub> are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, cyano, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, carboxyalkyl, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, aralkylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino, aralkylcarbonylamino, alkylcarbonyl, aminosulfonyl, alkylaminosulfonyl, and alkylsulfonyl;

R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently selected from the group consisting of hydrogen, halo, haloalkyl, alkyl, alkenyl, alkynyl, hydroxyalkyl,

aminoalkyl, carboxyalkyl, alkoxyalkyl, nitro, amino, ureido, cyano, acylamino, amide, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, carbonylamido and alkylthiol;

R<sub>10</sub> is selected from the group consisting of amino, alkyl, alkenyl, alkynyl, OR<sub>11</sub>, alkylamino, dialkylamino, alkenylamino, dialkylaminoalkenyl, cycloalkyl, heterocycle, heteroaryl, aryl, aralkyl, arylalkenyl, arylalkynyl, and cycloalkylalkylamino;

R<sub>11</sub> is selected from the group consisting of hydrogen, optionally substituted alkyl, and an alkalimetal; and

provided that:

- 1) when Het is (ii), and X is O, then R<sub>10</sub> is not alkyl, aralkyl, aryl or OR<sub>11</sub>;
- 2) when Het is (i) or (ii), then X is not NR<sub>9</sub>;
- 3) when Het is (iii), then X is not CH<sub>2</sub>; and
- 4) when Het is (iii), and X is O, then R<sub>10</sub> is not OR<sub>11</sub>.

2. A compound of claim 1, wherein R<sub>1</sub> is selected from the group consisting of an alkyl optionally substituted by halogen, hydroxy, carbamoyloxy, C<sub>1-6</sub> acyl, C<sub>1-6</sub> alkylsulfonylamino, aryl, or aminocarbonyl; C(O)R<sub>10</sub>; CH<sub>2</sub>C(O)R<sub>10</sub>; or SO<sub>2</sub>R<sub>10</sub>, wherein R<sub>10</sub> is selected from the group consisting of C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, OR<sub>11</sub>, amino, C<sub>1-6</sub> alkylamino, di(C<sub>1-6</sub>)alkylamino, C<sub>2-6</sub> alkenylamino, heterocycle and mono- and di-(C<sub>1-6</sub>)alkylaminoalkenyl, and R<sub>11</sub> is selected from the group consisting of hydrogen, optionally substituted alkyl, and an alkalimetal.

3. A compound of claim 2, wherein R<sub>10</sub> is selected from the group consisting of C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, OR<sub>10</sub>, amino, C<sub>1-6</sub> alkylamino, di(C<sub>1-6</sub>)alkylamino, C<sub>2-6</sub> alkenylamino, di(C<sub>1-6</sub>)alkylamino(C<sub>2-6</sub>)alkenyl, N-morpholinyl, N-pyrrolidinyl, and N-piperazinyl.

4. A compound of claim 3, wherein R<sub>2</sub> and R<sub>3</sub> are independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl,

C<sub>2</sub>-C<sub>6</sub> alkynyl, amino(C<sub>1</sub>-C<sub>6</sub>)alkyl, amino, C<sub>1</sub>-C<sub>6</sub> alkylthio, cyano, C<sub>1</sub>-C<sub>6</sub> alkylsulfinyl, hydroxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, aminocarbonyl, C<sub>1</sub>-C<sub>6</sub> alkylaminocarbonyl, C<sub>6</sub>-C<sub>10</sub> arylaminocarbonyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>1</sub>-C<sub>6</sub>)alkylaminocarbonyl, C<sub>1</sub>-C<sub>6</sub> alkylcarbonylamino, C<sub>6</sub>-C<sub>10</sub> arylcarbonylamino, and C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>1</sub>-C<sub>6</sub>)alkylcarbonylamino.

5. A compound of claim 3, wherein R<sub>2</sub> and R<sub>3</sub> are independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, amino(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>1</sub>-C<sub>6</sub> alkylthio and aminocarbonyl.

6. A compound of claim 1, wherein R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently selected from the group consisting of hydrogen, halo, halo(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl, hydroxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, amino(C<sub>1</sub>-C<sub>6</sub>)alkyl, carboxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, nitro, amino, C<sub>1</sub>-C<sub>6</sub> acylamino, amide, hydroxy, thiol, C<sub>1</sub>-C<sub>6</sub> acyloxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, carboxy, carbonylamido and C<sub>1</sub>-C<sub>6</sub> alkylthiol.

7. A compound of claim 1, wherein R<sub>1</sub> or R<sub>2</sub> is C(O)R<sub>10</sub> or SO<sub>2</sub>R<sub>10</sub>.

8. A compound of claim 7, wherein where R<sub>10</sub> is amino or C<sub>1-6</sub> alkyl.

9. A compound of claim 8, wherein X is O or S.

10. A compound of claim 9, wherein:

R<sub>5</sub> and R<sub>6</sub> are each hydrogen;

R<sub>3</sub> and R<sub>4</sub> are both H; and

R<sub>7</sub> and R<sub>8</sub> are selected from the group consisting of hydrogen, halo, halo(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl, hydroxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, amino(C<sub>1</sub>-C<sub>6</sub>)alkyl, carboxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, nitro,

amino, C<sub>1</sub>-C<sub>6</sub> acylamino, amide, hydroxy, thiol, C<sub>1</sub>-C<sub>6</sub> acyloxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, carboxy, carbonylamido and C<sub>1</sub>-C<sub>6</sub> alkylthiol.

11. A compound of claim 10, wherein Het is (i).
12. A compound of claim 10, wherein Het is (ii).
13. A compound of claim 10, wherein Het is (iii).
14. A compound of claim 10, wherein Het is (iv).

15. A compound of claim 1, wherein:

Het is (i), (ii), (iii) or (vi);

R<sub>1</sub> is C(O)R<sub>10</sub>, CH<sub>2</sub>C(O)R<sub>10</sub>, or SO<sub>2</sub>R<sub>10</sub>;

X is O or S;

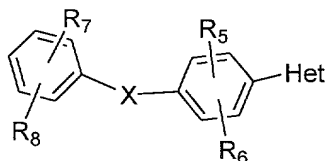
R<sub>10</sub> is amino, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, or a heterocycle selected from the group consisting of N-morpholinyl, N-pyrrolidinyl and N-piperazinyl;

R<sub>2</sub>, and R<sub>3</sub> are independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkylthio or C<sub>1</sub>-C<sub>6</sub> alkylsulfinyl,

R<sub>5</sub> and R<sub>6</sub> are as defined above and are preferably hydrogen, and

R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, halo, halo(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl, hydroxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, amino(C<sub>1</sub>-C<sub>6</sub>)alkyl, carboxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, nitro, amino, C<sub>1</sub>-C<sub>6</sub> acylamino, amide, hydroxy, thiol, C<sub>1</sub>-C<sub>6</sub> acyloxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, carboxy, carbonylamido and C<sub>1</sub>-C<sub>6</sub> alkylthiol.

16. A compound of Formula I:

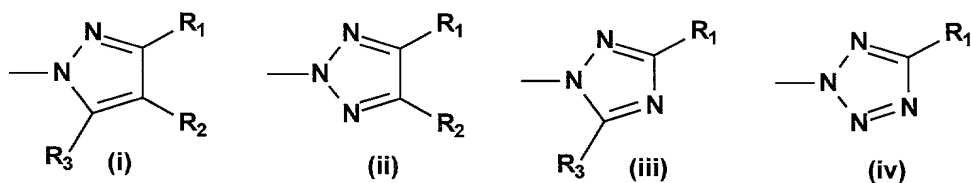


*I*

or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is O or S;

Het is a heteroaryl selected from the group consisting of



R<sub>1</sub> is C(O)R<sub>10</sub>, CH<sub>2</sub>C(O)R<sub>10</sub>, or SO<sub>2</sub>R<sub>10</sub> wherein R<sub>10</sub> is amino, alkyl, N-morpholinyl, N-pyrrolidinyl or N-piperazinyl, all of which can be optionally substituted;

R<sub>2</sub> and R<sub>3</sub> are independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkylthio or C<sub>1</sub>-C<sub>6</sub> alkylsulfinyl;

R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, halo, halo(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl, hydroxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, amino(C<sub>1</sub>-C<sub>6</sub>)alkyl, carboxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, nitro, amino, C<sub>1</sub>-C<sub>6</sub> acylamino, amide, hydroxy, thiol, C<sub>1</sub>-C<sub>6</sub> acyloxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, carboxy, carbonylamido and C<sub>1</sub>-C<sub>6</sub> alkylthiol;

provided that:

- 1) when Het is (ii), and X is O, then R<sub>10</sub> is not alkyl, aralkyl, aryl or OR<sub>11</sub>;  
and
- 2) when Het is (iii), and X is O, then R<sub>10</sub> is not OR<sub>11</sub>.

17. A pharmaceutical composition, comprising the compound of claim 1 or 16 and a pharmaceutically acceptable carrier or diluent.

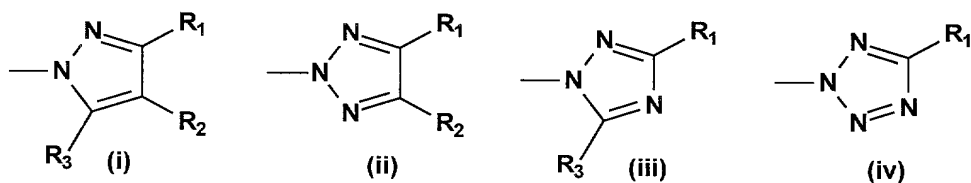
18. A method of treating a disorder responsive to the blockade of sodium channels in a mammal suffering therefrom, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula *I*:



or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is one of O, S, NR<sub>9</sub>, CH<sub>2</sub>, NR<sub>9</sub>C(O), or C(O)NR<sub>9</sub>, where R<sub>9</sub> is hydrogen or C<sub>1</sub>-C<sub>10</sub> alkyl;

Het is a heteroaryl selected from the group consisting of



R<sub>1</sub> is selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted heteroaryl, C(O)R<sub>10</sub>, CH<sub>2</sub>C(O)R<sub>10</sub>, S(O)R<sub>10</sub>, and SO<sub>2</sub>R<sub>10</sub>;

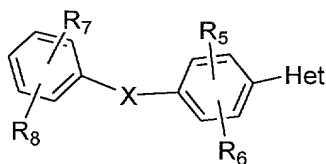
R<sub>2</sub> and R<sub>3</sub> are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, cyano, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, carboxyalkyl, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, aralkylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino, aralkylcarbonylamino, alkylcarbonyl, aminosulfonyl, alkylaminosulfonyl, and alkylsulfonyl;

R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently selected from the group consisting of hydrogen, halo, haloalkyl, alkyl, alkenyl, alkynyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, alkoxyalkyl, nitro, amino, ureido, cyano, acylamino, amide, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, carbonylamido and alkylthiol;

R<sub>10</sub> is selected from the group consisting of amino, alkyl, alkenyl, alkynyl, OR<sub>11</sub>, alkylamino, dialkylamino, alkenylamino, dialkylaminoalkenyl, cycloalkyl, heterocycle, heteroaryl, aryl, aralkyl, arylalkenyl, arylalkynyl, and cycloalkylalkylamino;

R<sub>11</sub> is selected from the group consisting of hydrogen, optionally substituted alkyl, and an alkalimetal.

19. A method for treating, preventing or ameliorating neuronal loss following global and focal ischemia; treating, preventing or ameliorating neurodegenerative conditions; treating, preventing or ameliorating pain or tinnitus; treating, preventing or ameliorating manic depression; providing local anesthesia; or treating arrhythmias, or treating convulsions, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula *I*:

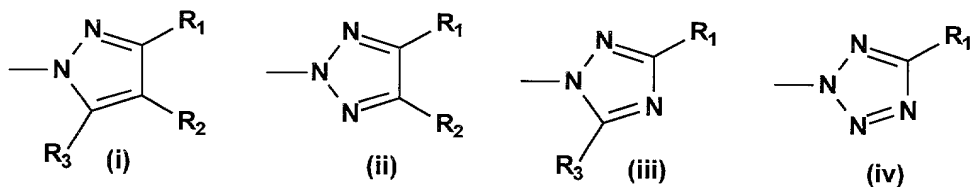


*I*

or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is one of O, S, NR<sub>9</sub>, CH<sub>2</sub>, NR<sub>9</sub>C(O), or C(O)NR<sub>9</sub>, where R<sub>9</sub> is hydrogen or C<sub>1</sub>-C<sub>10</sub> alkyl;

Het is a heteroaryl selected from the group consisting of



R<sub>1</sub> is selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted heteroaryl, C(O)R<sub>10</sub>, CH<sub>2</sub>C(O)R<sub>10</sub>, S(O)R<sub>10</sub>, and SO<sub>2</sub>R<sub>10</sub>;

R<sub>2</sub> and R<sub>3</sub> are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, cyano, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, carboxyalkyl, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, aralkylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino, aralkylcarbonylamino, alkylcarbonyl, aminosulfonyl, alkylaminosulfonyl, and alkylsulfonyl;

R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently selected from the group consisting of hydrogen, halo, haloalkyl, alkyl, alkenyl, alkynyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, alkoxyalkyl, nitro, amino, ureido, cyano, acylamino, amide, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, carbonylamido and alkylthiol;

R<sub>10</sub> is selected from the group consisting of amino, alkyl, alkenyl, alkynyl, OR<sub>11</sub>, alkylamino, dialkylamino, alkenylamino, dialkylaminoalkenyl, cycloalkyl, heterocycle, heteroaryl, aryl, aralkyl, arylalkenyl, arylalkynyl, and cycloalkylalkylamino;

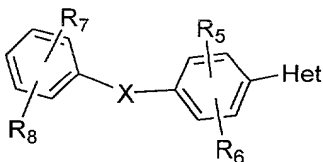
R<sub>11</sub> is selected from the group consisting of hydrogen, optionally substituted alkyl, and an alkalimetal.

20. The method of claim 19, wherein the method is for treating, preventing or ameliorating pain and said pain is one of neuropathic pain, surgical pain or chronic pain.



21. A method of alleviating or preventing seizure activity in an animal subject, comprising administering to a mammal in need of such treatment an effective amount of a compound of claim 1 or 16.

22. A compound of Formula I:

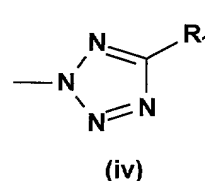
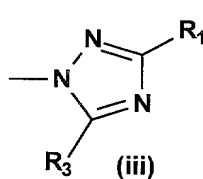
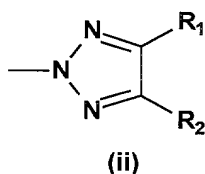
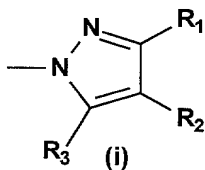


I

or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is O or S;

Het is a heteroaryl selected from the group consisting of



R<sub>1</sub> is C(O)R<sub>10</sub>, wherein R<sub>10</sub> is amino, N-morpholinyl, N-pyrrolidinyl or N-piperazinyl, all of which can be optionally substituted

R<sub>2</sub> and R<sub>3</sub> are independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkylthio or C<sub>1</sub>-C<sub>6</sub> alkylsulfinyl;

R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, halo, halo(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl, hydroxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, amino(C<sub>1</sub>-C<sub>6</sub>)alkyl, carboxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, nitro, amino, C<sub>1</sub>-C<sub>6</sub> acylamino, amide, hydroxy, thiol, C<sub>1</sub>-C<sub>6</sub> acyloxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, carboxy, carbonylamido and C<sub>1</sub>-C<sub>6</sub> alkylthiol.

23. A compound of claim 22, wherein X is O.